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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/297,668	05/06/99	GERSHONI J	27/135

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EXAMINER	
FORMAN, B	
ART UNIT	**PAPER NUMBER**
1655	7

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/297,668	GERSHONI ET AL.	
	Examiner	Art Unit	
	BJ Forman	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 November 2000* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *112-143* is/are pending in the application.

4a) Of the above claim(s) *112-136* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *137-143* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☒ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

1. Applicant's election without traverse of Group IV claims 137-143 filed 24 November 2000 in Paper No. 6 is acknowledged. The amendments to Claim 137 filed in Paper No. 6 are acknowledged. Claims 112-136 are withdrawn from further consideration. Claims 137-143 are discussed below.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 137-143 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 137-143 are indefinite in Claim 137 for the recitation "conformational peptide of a discontinuous epitope" because "conformational peptide" is not standard scientific terminology and therefore it is unclear what limitations are imposed upon the peptide. It is suggested that the claim be amended to clarify e.g. define "conformational peptide".

b. Claims 137-143 are indefinite in Claim 137, step (a)(i) for the recitation "DNA fragments corresponding to at least a portion of a genome of the organism" because "corresponding" is a non-specific relational term and therefore the relationship between the "DNA fragments" and the "genome" is undefined. It is suggested that Claim 137 be amended to define the relationship between the "DNA fragments" and the "genome" e.g. replace "corresponding to" with "from".

c. Claims 137-143 are indefinite in Claim 137, step (c) for the recitation "conformational fragments" because "conformational" lacks proper antecedent basis in step (a) of the claim

which recites "DNA fragments". It is suggested that Claim 137 be amended to provide proper antecedent basis e.g. replace "conformational" with "DNA".

d. Claims 137-143 are further in definite in Claim 137, step (c) for the recitation "said discontinuous library" because the library lacks proper antecedent basis in the claim. It is suggested that Claim 137, step (c) be amended to provide proper antecedent basis i.e. replace "said" with "a".

e. Claims 137-143 are indefinite in Claim 137, step (e) for the recitation "obtaining the conformational peptide" because "obtaining" is a non-specific activity and therefore it is unclear how the peptide is "obtained". The recitation is further indefinite because "obtaining" lacks proper antecedent basis in the method for "preparing". It is suggested that Claim 137 be amended to clarify and provide proper antecedent basis e.g. replace "obtaining" with "preparing".

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 137-143 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gritz et al. (U.S. Patent No. 5,691,170, issued 25 November 1997) in view of Mandeville et al. (U.S. Patent No. 6,031,071, filed 24 January 1996).

Regarding Claim 137, Gritz et al. teach a method for preparing a peptide of a discontinuous epitope (Column 9, lines 54-57) of a single biological unit of an organism which is the HIV env gene (Example 3) the method comprising the steps of: providing a plurality of

DNA fragments corresponding to at least a portion of a genome by digesting said at least a portion of said genome of the organism to form said plurality of fragments; ligating said plurality of fragments to form at least one ligated fragment i.e. plasmid pAbT4075 comprising the HIV-1 BH10 env gene fragment and plasmids pAbT4082 comprising the HIV-1 RF env gene fragment (Example 3, Column 13, lines 35-46); at least partially digesting said at least one ligated fragments to form a plurality of fragments coding for the discontinuous epitope of the single biological unit i.e. plasmid pAb4085 comprising the HIV-1 BH10 env gene fragment plus the HIV-1 RF env gene fragment (Column 13, lines 59-62 and Fig. 6); inserting said discontinuous epitope into an expression system i.e. viral genome (Example 4, Column 13, lines 65-67 and Fig. 7) and they teach obtaining a peptide from said expression system wherein the presence of the peptide is confirmed by HIV-specific antibody recognition (Example 7, Table 1). Gritz et al. teach the method wherein said plurality of fragments coding for the discontinuous epitope are inserted into the vial genome wherein following a recombination event a discontinuous epitope is formed and wherein number of different recombination events occur to thereby form a discontinuous library i.e. a diverse set of chimeric env genes (Example 4, Column 14, lines 17-20) but they do not teach forming said discontinuous library prior to inserting said library in to said expression system. Mandeville et al. teach a similar method for preparing a conformational peptide of a discontinuous epitope i.e. "peptides that represent discontinuous amino acids" (Column 7, lines 33-37) the method comprising: providing a plurality of DNA fragments corresponding to at least a portion of a genome of an organism, ligating said plurality of fragments to form at least one ligated fragment thereby forming a discontinuous library; inserting said library into an expression system wherein each discontinuous epitope of the library is inserted 5' of a sequence encoding a coat protein and obtaining the peptide from said expression system (Column 6, lines 42-58). It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the insertion followed by recombination to form the discontinuous library as

taught by Gritz et al. with the direct insertion of the discontinuous epitopes 5' to a coat protein whereby expressed epitopes are displayed on the bacteriophage for the known benefits of phage display techniques i.e. facility of peptide selection and for the expected benefit of screening the displayed discontinuous epitopes to identify the best diversity of epitopes binding to any ligand and using the displayed discontinuous epitopes as an immunogen to produce antibodies as taught by Mandeville et al. (Column 2, lines 35-53).

Regarding Claim 138, Gritz et al. teach the method wherein said expression system comprise a plurality of bacteria (Column 14, lines 27-38) but they do not teach step (d) is performed by inserting each of said plurality of fragments of said discontinuous library into genetic material of said bacteria. Mandeville et al. teach a similar method for preparing a conformational peptide wherein step (d) is performed by inserting each of said plurality of fragments of said discontinuous library in to genetic material of said bacteria i.e. bacterial host cells are transformed with a bacteriophage expression vectors comprising the discontinuous library (Column 7, lines 14-21). It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the bacterial expression system of Gritz et al. with the bacteriophage expression system for their known benefits as a powerful tool for the selection of peptide sequences as taught by Mandeville et al. (Column 2, lines 48-53).

Regarding Claim 139, Gritz et al. teach the method wherein said expression system comprises a plurality of viral vectors and step (d) is performed by inserting each of said plurality of fragments of said discontinuous library into genetic material of each of said viral vectors (Column 13, lines 65-67) but they do not teach the viral vectors are phages. Mandeville et al. teach the similar method wherein said expression system comprises a plurality of viral vectors which are phages and step (d) is performed by inserting each of said plurality of fragments of said discontinuous library into genetic material of each of said phage (Column 7, lines 14-21). It would have been *prima facie* obvious to one of ordinary skill in the art at the

time the claimed invention was made to modify the bacterial expression system of Gritz et al. with the bacteriophage expression system for their known benefits as a powerful tool for the selection of peptide sequences as taught by Mandeville et al. (Column 2, lines 48-53).

Regarding Claim 140, Gritz et al. al. teach the method wherein each of said plurality of fragments is a portion of the HIV env gene (Example 3, Column 13), but they do not teach the fragments are cloned in to a phage gene coding for a coat protein. Mandeville et al. teach the similar method wherein each of said plurality of fragments is cloned in to a phage gene coding for a coat protein such that the peptide is displayed by said coat protein (Column 6, lines 42-49). It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the bacterial expression system of Gritz et al. with the bacteriophage system of Mandeville et al. wherein the expressed fragments are displayed on bacteriophage for the known benefits of phage display i.e. powerful selection tool for identifying peptides which bind to pre-selected targets, for identifying target analogs and for antibody production (Column 6, lines 19-41).

Regarding Claim 141, Mandeville et al. teach the method where in said plurality of phages are filamentous phages and said coat protein is pIII (Column 4, lines 33-36). It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the bacterial expression system of Gritz et al. with the bacteriophage system of Mandeville et al. wherein the expressed fragments are displayed for the known benefits of phage display i.e. powerful selection tool for identifying peptides which bind to pre-selected targets, for identifying target analogs and for antibody production (Column 6, lines 19-41).

Regarding Claim 142, Gritz et al. teach a conformational peptide of a single biological unit of an organism i.e. HIV env gene (Example 7, Column 16) wherein the peptide is produced by expressing a discontinuous epitope library and wherein the production of the peptide is confirmed by anti-HIV env antibody recognition (Column 16, Table 1) but they do not teach

producing the peptide by forming a discontinuous library prior to inserting said library into said expression system. Mandeville et al. teach the similar method for preparing a conformational peptide of a discontinuous epitope (Column 7, lines 33-37) wherein each discontinuous epitope of the library is inserted 5' of a sequence encoding a coat protein and obtaining the peptide from said expression system (Column 6, lines 42-58). It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the insertion followed by recombination to form the discontinuous library of Gritz et al. with the direct insertion of the discontinuous epitopes 5' to a coat protein whereby expressed epitopes are displayed as a portion of an outer structural protein of the bacteriophage for the expected benefit of screening the displayed discontinuous epitopes to identify the best diversity of epitopes binding to any ligand and using the displayed discontinuous epitopes as an immunogen to produce antibodies as taught by Mandeville et al. (Column 4, lines 20-30).

Regarding Claim 143, Gritz et al. teach a method for vaccinating a subject i.e. a rabbit, against an organism i.e. HIV (Column 9, lines 36-39) comprising the steps of: preparing a conformational peptide of a single biological unit of the organism according to the method of Claim 137 (Example 3, Column 13); placing said peptide in a vaccine carrier i.e. poxvirus (Column 9, lines 44-49); administering said conformational peptide in said vaccine carrier to the subject (Example 7, Column 16) but they do not teach producing the peptide by forming a discontinuous library prior to inserting said library into said expression system. Mandeville et al. teach the similar method for preparing a conformational peptide of a discontinuous epitope (Column 7, lines 33-37) wherein each discontinuous epitope of the library is inserted 5' of a sequence encoding a coat protein and obtaining the peptide from said expression system (Column 6, lines 42-58). It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the peptide production by random recombination of Gritz et al. with specific recombinatory techniques to display the peptide

within a bacteriophage coat protein for the expected benefit of using the produced peptide "as is" as an antigen in a vaccine composition as taught by Mandeville et al. (Column 2, lines 51-52).

Conclusion

6. No claim is allowed.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878. The examiner can normally be reached on 6:45 TO 4:15.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

BJ Forman, Ph.D.
December 4, 2000

W. Gary Jones
Supervisory Patent Examiner
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12/4/00